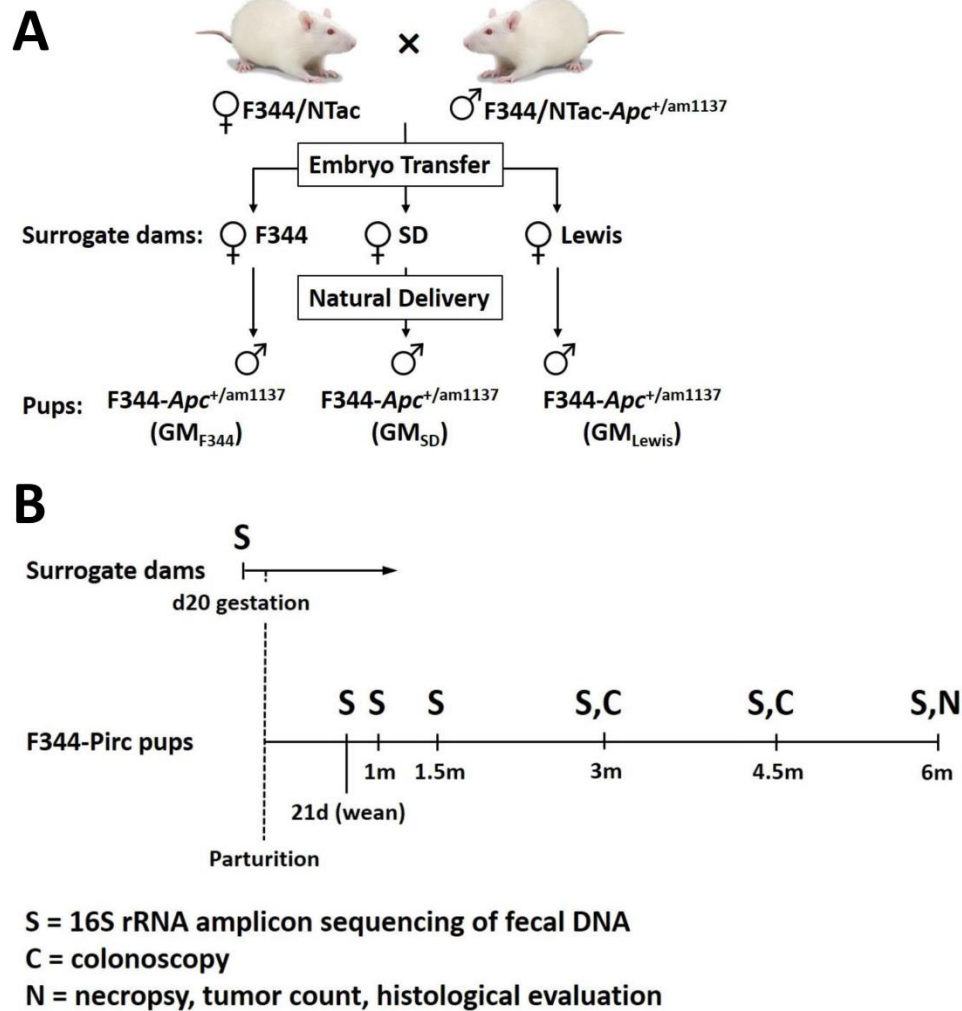
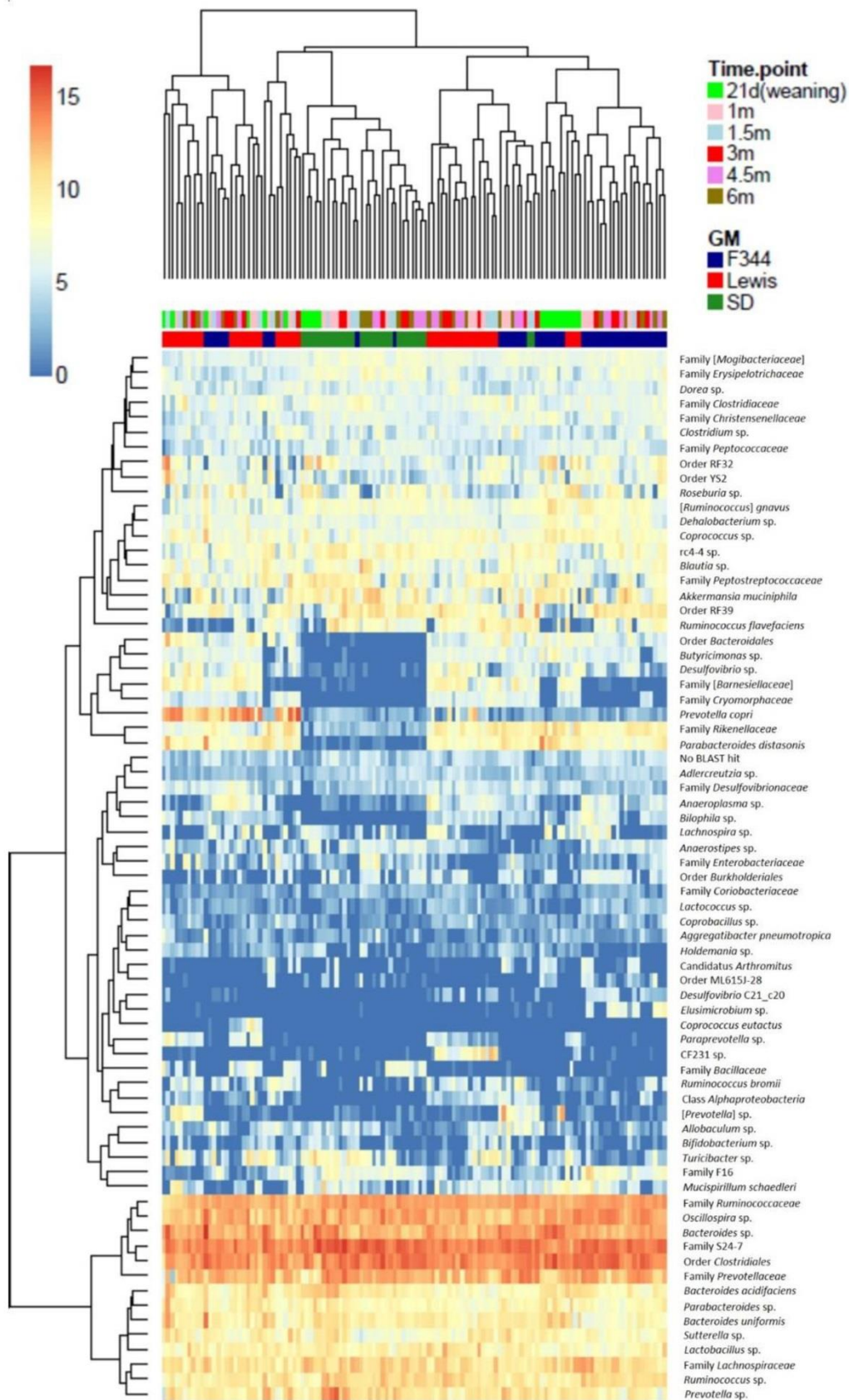


# Differential susceptibility to colorectal cancer due to naturally occurring gut microbiota

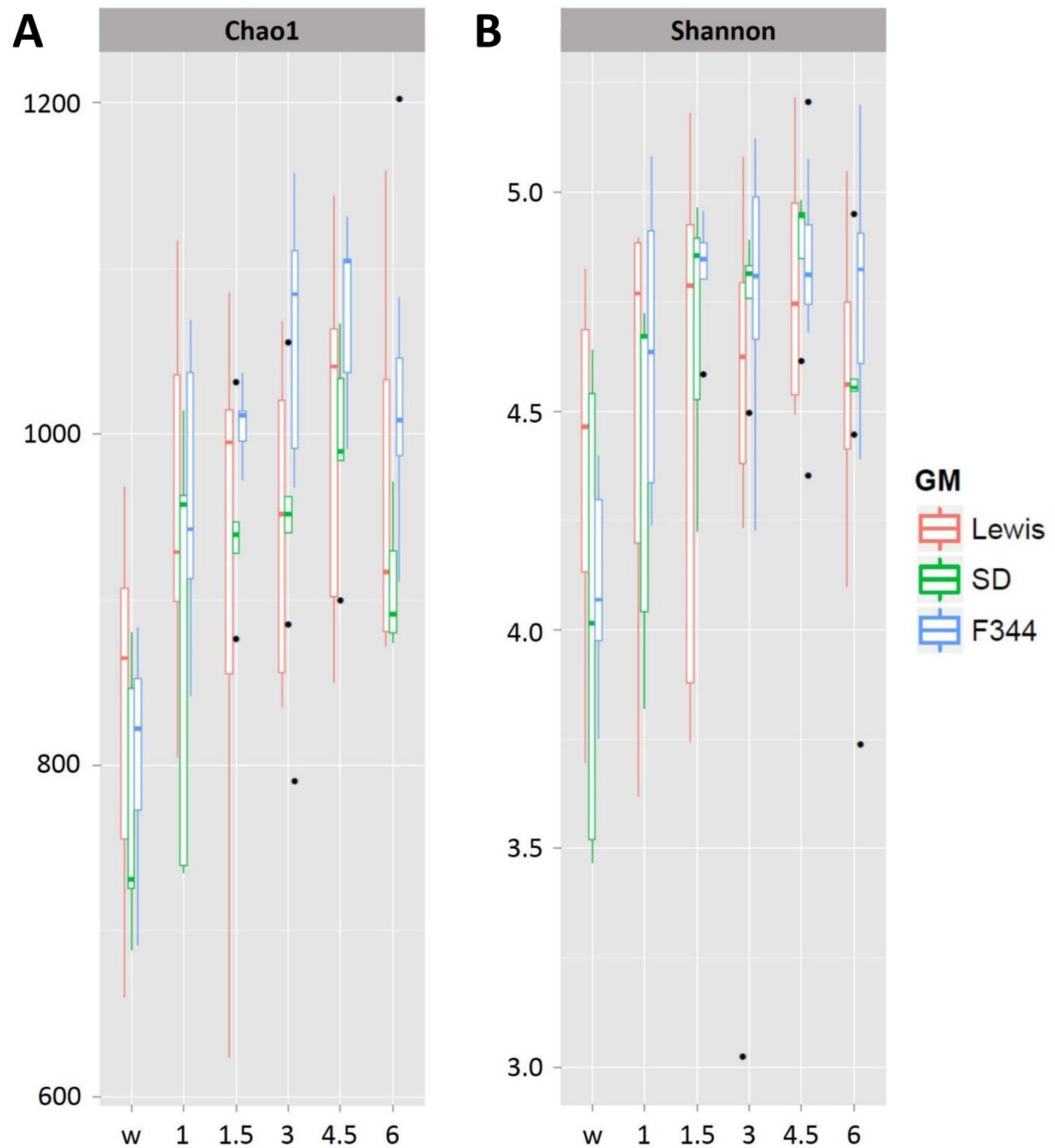
## Supplementary Material



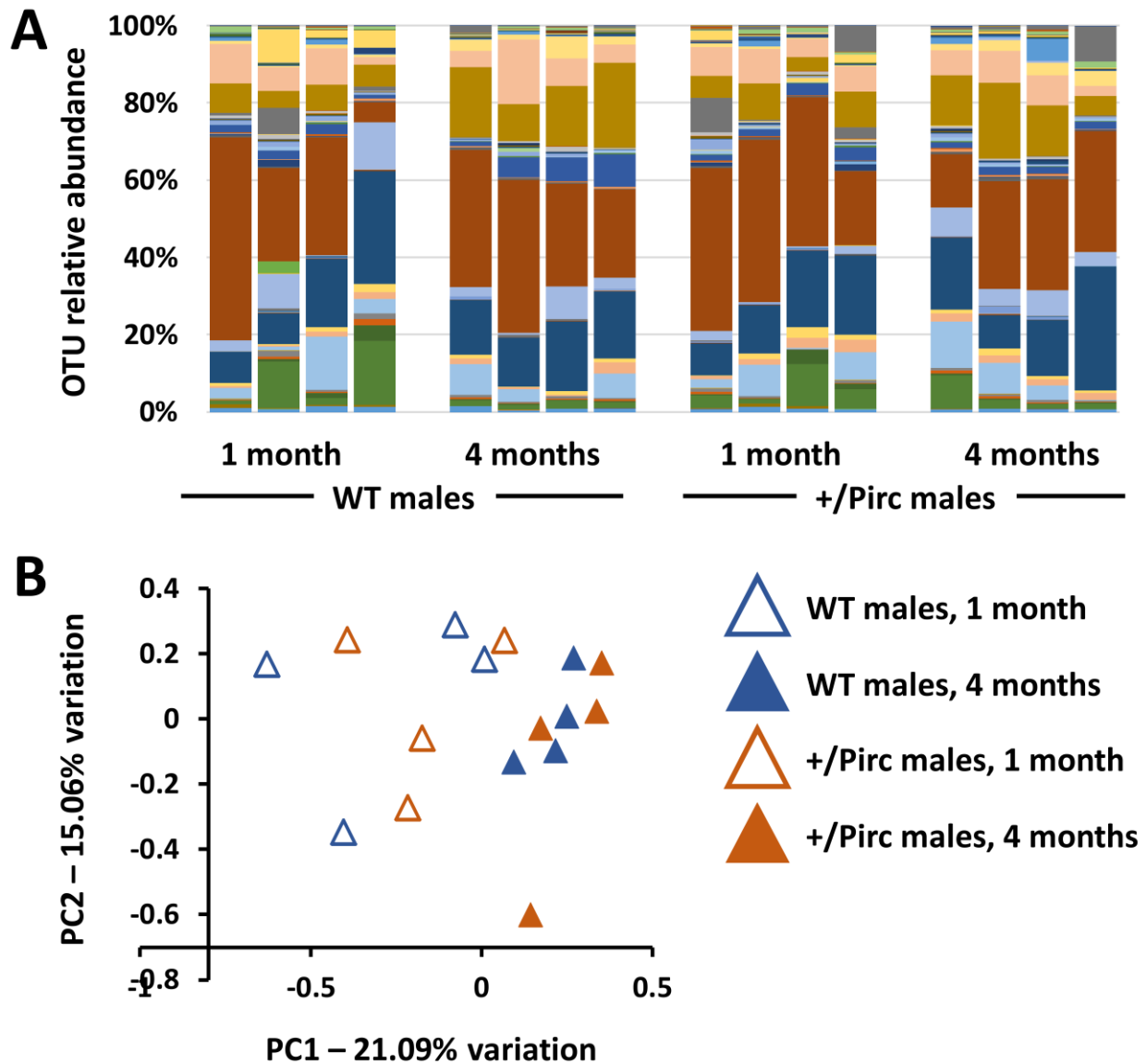
**Supplementary Fig. S1: Experimental design used to generate isogenic F344-Pirc rats with different gut microbiota.** Schematic showing the breeding and embryo transfer scheme used to generate isogenic F344-Pirc rats harboring different gut microbiota profiles (**A**), and timeline depicting sample collection and procedural time points (**B**).



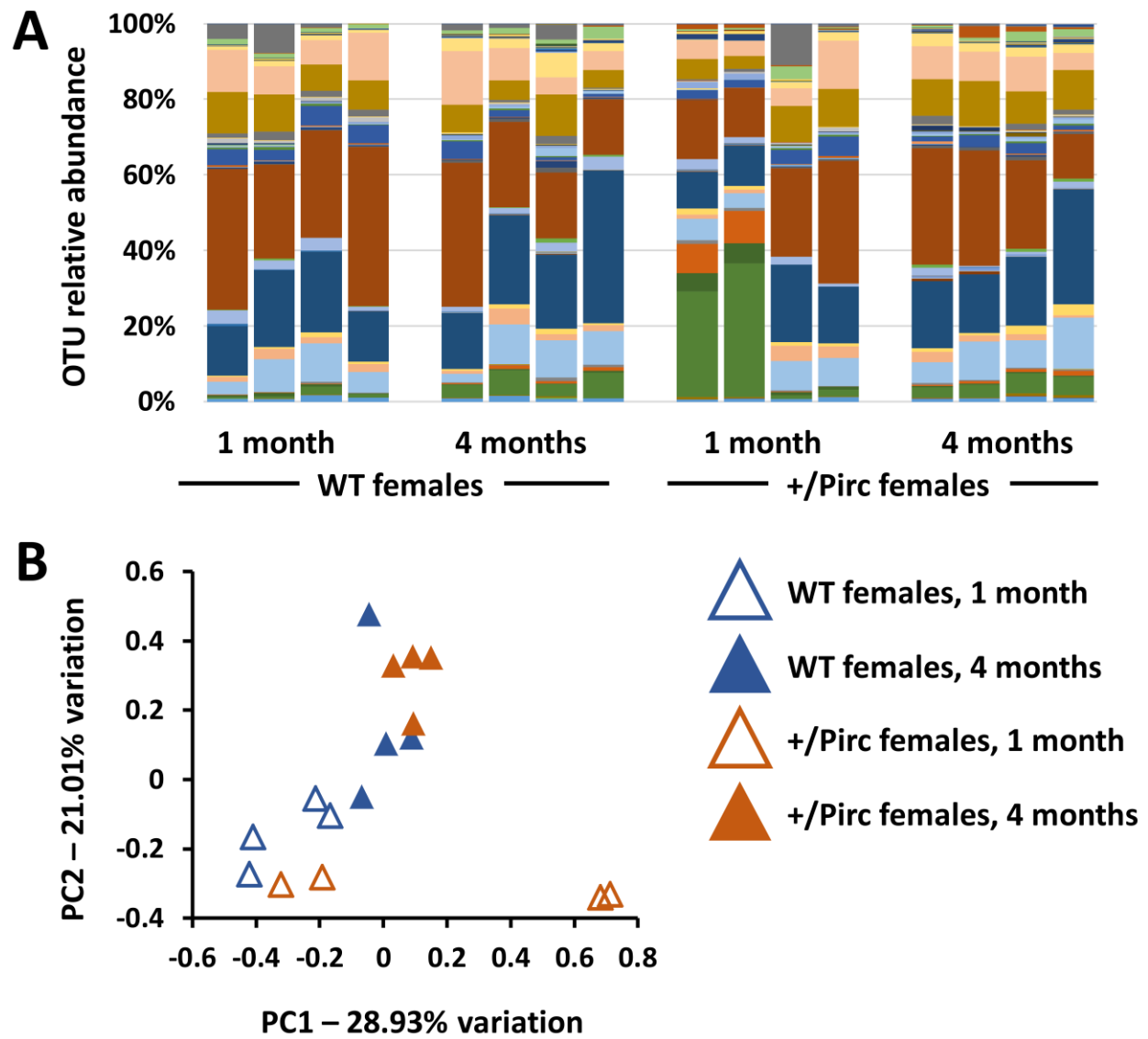
**Supplementary Fig. S2: Hierarchical cluster analysis of male F344-Pirc rats.** Agglomerative hierarchical clustering analysis of the 71 consistently detected operational taxonomic units (OTUs) in the GM of male F344-Pirc pups born to F344, SD, or Lewis surrogate dams, at weaning (21d), 1 month (1m), 1.5m, 3m, 4.5m, and 6m of age. Color intensity shows  $\log_2$ -transformed normalized abundance of OTUs in each sample (bar at upper left). Operational taxonomic units are listed at right, time of sampling and identity of surrogate dam are denoted by color-coded bars at top (legend at upper right).



**Supplementary Fig. S3: Diversity of fecal microbiota.** Box plots of Chao1 (A) and Shannon (B) estimates of microbial diversity plotted by time point. Data points are colored to indicate GM profile (GM<sub>F344</sub>, blue; GM<sub>SD</sub>, green; GM<sub>Lewis</sub>, red).



**Supplementary Fig. S4: Influence of the +/Pirc genotype on the gut microbiota in male rats.** Bar charts showing the relative abundance of operational taxonomic units (OTUs) detected in the feces of non-rederived male wild-type (WT) and heterozygous (+/Pirc) littermates ( $n = 4/\text{group}$ ), collected at 1 and 4 months of age (**A**); principal component analysis of the samples shown in A, demonstrating clustering of samples by age, rather than genotype (**B**; legend at right).



**Supplementary Fig. S5: Influence of the +/Pirc genotype on the gut microbiota in female rats.** Bar charts showing the relative abundance of operational taxonomic units (OTUs) detected in the feces of non-rederived female wild-type (WT) and heterozygous (+/Pirc) littermates ( $n = 4/\text{group}$ ), collected at 1 and 4 months of age (**A**); principal component analysis of the samples shown in A, demonstrating clustering of samples by age, rather than genotype (**B**; legend at right).

**Supplementary Table 1: Summary of rederivation attempts resulting in F344-Pirc offspring.** Number and genotype of male and female offspring born from each round of embryo transfer into F344/NHsd (F344), Crl:SD (SD), and LEW/SsNHsd (Lewis) surrogate dams. ID = dam ear-tag number, DOB = date of birth.

Surrogate dams				Male pups		Female pups	
Background	ID	DOB	# pups	WT	+/Pirc	WT	+/Pirc
F344/NHsd	270RA	9/12/13	3	0	1	unknown	
	049RG	9/17/13	5	0	1	unknown	
	795RC	10/23/13	11	4	2	unknown	
	349RJ	12/11/13	12	3	1	unknown	
	649RJ	2/19/14	11	2	3	unknown	
Crl:SD	794RC	10/23/13	11	1	5	1	4
LEW/SsNHsd	235RH	8/27/13	7	2	1	unknown	
	100RH	9/3/13	10	3	1	unknown	
	050RG	9/17/13	6	0	2	unknown	
	424RD	10/16/13	13	0	3	5	5
	131RH	10/30/13	6	2	1	1	2